

BfR2GO

ISSUE 2/2023



PLANT INGREDIENTS

**NATURAL
DEFENCES**

POISONING

COLLECTING DATA –
SAVING LIVES

GENE CUTTING

DETECTING
CHANGES

EMBRYOIDS

UNDERSTANDING
THE BEGINNING



FOODIES WANTED

Vegan, vegetarian, pescetarian or a mixed diet: how do these diets affect our health? This is what the COPLANT study is investigating on a large scale. Researchers are looking for around 6,000 people to participate. Interested?

More information:

www.bfr.bund.de/en/coplant-study.html



COPLANT


Only a fraction of consumers in Germany feels well informed about plant toxins.

—
Results of a representative
BfR survey





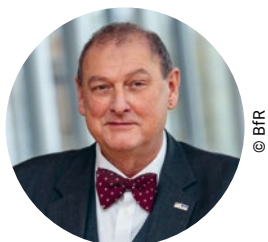
How did governments and institutions communicate during the COVID-19 pandemic? And how did people react on social media? This is what the MIRKKOMM research project is looking at. “Clarifying terms such as ‘R number’ and ‘incidence’ was particularly challenging. Not all citizens were able to understand the communication at the same level. Many yearned for supposedly simple answers,” says BfR scientist Dr Annett Schulze, who coordinates the network project. “The aim of MIRKKOMM is to derive standards for scientifically based communication that is both clear and trustworthy.” Initial research results were presented at the exhibition on communication during the pandemic “#Krisenalltag – Kommunikation in der Pandemie” in Berlin. The MIRKKOMM project will run until September 2024 and is funded by the Federal Ministry of Education and Research (BMBF).

 More information



Project website
MIRKKOMM (in German)

Editorial



Dear readers,

If you have time to read just one article in the new BfR2GO, it should be our lead story on plant ingredients. The article highlights the world of plants' "green chemistry" – and how important risk assessment is here, too. For example, plants boast a wide variety of chemical defences, which they produce to spoil the appetite of insects, microorganisms and other predators. And then there are the healthy plant ingredients. Sometimes you'll even find the good and the poisonous in the same substance. Just think of essential oils or alkaloids such as morphine.

"Purely herbal" is a label that still works wonders – at least for selling food supplements, as one example. An online survey carried out by the BfR shows how little people know about plant ingredients. At least this issue of BfR2GO will provide some answers! And we also provide information on mould toxins and the national poisoning register. For a quick detox after reading so much about toxicology, I recommend our interview with the unorthodox comedian Vince Ebert. So take a look at the "other side" of plants, and the many sides of the BfR, and prepare for some surprises!

Professor Dr Dr Andreas Hensel
BfR President

**Assessment.
Research.
Communication.**

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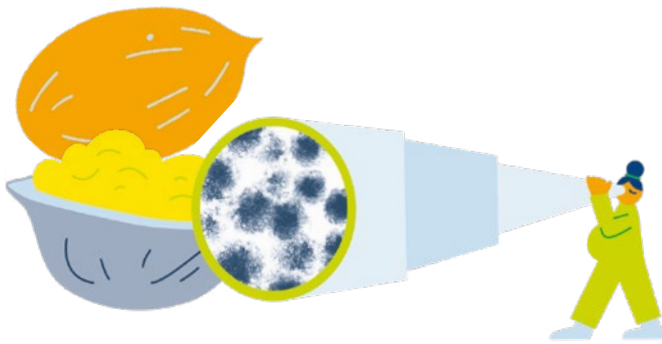


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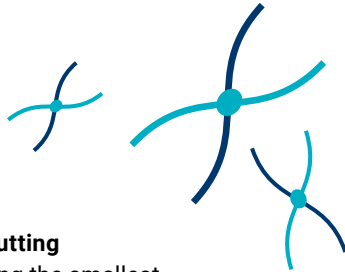
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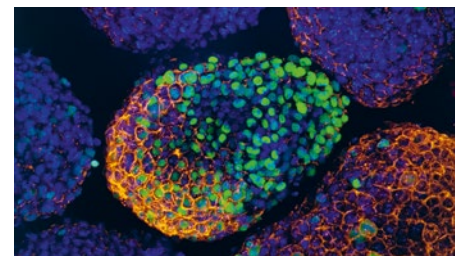


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Natural defences

Representative surveys sometimes show a high level of public concern about health risks from man-made chemicals in food. Nature's kitchen of poisons is often overlooked.

There it is – ragwort. It appears innocent and inconspicuous with its green leaves, yellow flowers and slender stem rising no more than a metre from the ground. If a predator were to pass by in search of food, the plant would appear to have nothing to offer at first glance. No thorns or optical tricks to confuse or command respect. Yet ragwort is greatly feared by farmers because it can kill adult horses and cattle if they eat it in the field or if it is fed to them in their troughs in the form of contaminated feed. This is because

of the pyrrolizidine alkaloids it produces, which can damage the liver and cause cancer, even in humans. But more on that later.

SMALL BUT MIGHTY

Welcome to the vast maze of “secondary plant ingredients”. These are all substances that plants produce but do not need for their own nutrition. Yet they are essential for their survival. On the one hand, plants have to use attractants and messenger substances or bright signal colours





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The plant kingdom offers a huge repertoire of substances, many of which are used by humans.

to invite insects to visit, take their pollen and spread it. On the other hand, they have to defend themselves against various attackers with bitter substances or poisons. This can only be done on the spot because of their roots, so they have to come from the plants themselves. A wide variety of substances have developed in the course of evolution. Science provides insights into this exciting world.

HARD TO KEEP TRACK OF VARIETY

The plant kingdom offers a huge repertoire of substances, many of which are used by humans. They are said to improve circulation and metabolism, for example, or act as antioxidants to neutralise free radicals in our cells.

Nutritional science also generally refers to health-promoting properties – a varied, predominantly plant-based diet is recommended. This is easy today, given the abundance of plant-based foods from many regions of a globalised world.

Whether jackfruit from India or avocados from Peru, everything is always within reach simply by visiting the local supermarket or through home delivery with just a few clicks. However, considering this great diversity, only very few substances from the global plant kingdom can be comprehensively studied for their health risks. It is often helpful to know whether a particular food has been used as a safe food in a third country. For example, the European Novel Food

New trends, often fuelled by social media, can lead to health problems.



Ragwort: can cost the lives of adult cattle and horses.

© Cow: berdsigns, plants: schab, Valeriy Kirsanov @adobestock

Regulation requires that foreign foods have been used in at least one third country for at least 25 years as part of the customary diet of a significant number of people (more on the toxicological assessment of plant ingredients in the interview with Dr Benjamin Sachse on page 14).

INTOX INSTEAD OF DETOX

Some nutrition trends are not always covered by experience and research, for example, smoothies. Depending on the recipe, they contribute to a healthy nutrient supply with vitamins, minerals and fibre. However, new trends, often fuelled by social media, can lead to health problems. For example, when unusual plant parts, such as leaves, stems, peel, or seeds, end up in the blender along with the traditionally consumed plant parts. The plant ingredients are not homogenously distributed



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within it; concentrations can differ significantly; for example, while apricot and plum flesh can be enjoyed without any worry, the seeds contain cyanogenic glycosides that release highly toxic prussic acid in the digestive tract and can even lead to fatal poisoning in larger quantities.

Concentrated intake of a substance in a quantity that is usually not reached through normal consumption can also be problematic. Certain plant extracts that can be used in food supplements, among other things, are an example of this. Food supplements are legally considered to be food and as such do not require approval, even if they sometimes look similar or exactly the same as medicines. In contrast to food supplements, medicines have to go through an extensive approval

procedure before they can be used. A reliable health risk assessment is not easy if a food supplement contains highly concentrated extracts of plant ingredients: do they interact with each other or with certain medicines? Is even short-term intake a health risk or only long-term consumption? Delayed effects are often difficult to detect and there are usually large gaps in the data. One example is quercetin, a plant pigment widely found in fruits and vegetables. People consume only a few milligrams per day as part of a normal diet. However, quercetin is also used as an ingredient in food supplements, where the amount consumed can be several grams per day, depending on the preparation. Whether this really supports the immune system, as advertised, or rather has a negative impact on the body, is still largely

BfR-survey: Plant ingredients



8 %

rate their awareness of naturally occurring plant poisons in food as (very) good. 37 % answered "neutral/neither nor", while the majority (53 %) feel (very) poorly informed.

4 %

have heard of pyrrolizidine alkaloids, but most are completely unaware of the substances, which can damage the liver and are carcinogenic.

25 %

have never heard of plant toxins. Another quarter of respondents had, but did not know what it meant. 47 % were familiar with the term and meaning.

Online survey of 1,012 people in Germany, survey period: 7-11 August 2023

However, toxic ingredients can also sometimes be useful for plants, humans and animals.

open, as is the case with most substances of this kind.

WHAT THE POPULATION KNOWS

What do people in Germany know about these kinds of substances? This is what the German Federal Institute for Risk Assessment (BfR) has investigated. A representative population survey paints a clear picture. Only a fraction of consumers in Germany feels well informed about plant toxins. The results were scarcely better when it came to awareness of individual substances. With the exception of morphine and opiates, which were known to 61 % of the participants – which possibly also has something to do with their prominent role in the field of medicines and narcotics – the majority of respondents said they had

not heard of any of the substances mentioned. Coumarin, which is found in cinnamon, solanine, which is found in potatoes, and oxalates, which are found in spinach are relatively well known. The least known substances, including phasin, which is found in raw beans, were in the single-digit percentage range and are thus practically unknown to the population. Overall, only slightly more than a quarter of respondents said they were “(very) concerned” about natural plant poisons. The widespread unfamiliarity does not cause as much concern about health risks here as it does with other, often well-researched food safety topics, such as plant protection product residues.

BAD FOR HUMANS, GOOD FOR LLAMAS

However, toxic ingredients can also sometimes be useful for plants, humans or animals. The quinolizidine alkaloids produced by lupins can cause poisoning symptoms in humans, but they provide a good service to Bolivian llama breeders. They place the lupins in water containers in the sun so that the quinolizidine alkaloids they contain are transferred into the water. A few hours later, the natural shampoo with insect repellent for the llamas' fur is ready. It seems that there really is a herb for everything – you just need to know how to use it. —

More information



BfR information
“Plant ingredients”



“Natural substances are often more ruthless than artificial ones”

Dr Benjamin Sachse assesses at the BfR the health risks that can be posed by plant ingredients. He puts the topic into context in this BfR2GO interview.

Mr Sachse, artificially produced or naturally occurring – as a scientist, do you differentiate between the two when it comes to secondary plant ingredients?

As a toxicologist, I look at the toxicity of a substance and whether it might cause harmful effects. And natural substances are often even more “ruthless” than artificially produced ones.

Many substances that we often consume and perceive as very positive come from the plant world. Manufacturers also like to use them in their advertising. Is this okay or should we be more sceptical?

Not all substances that plants produce as a defence against animals or pathogens are harmful to humans. Many secondary plant ingredients are beneficial to us. Think of the bitter substances and essential oils found in spices, which are an integral part of our diet and stimulate appetite and digestion, for example.

However, we need to look at each substance individually – sometimes it is just the dose that makes the difference to health. For example, coumarin in certain types of cinnamon is harmful to the liver in high doses and may only occur in food to a limited extent.

Since you just brought it up: it is not just artificially produced chemicals that are subject to regulations and limits. What about natural plant substances?

In the EU, there are now legal limits for some harmful plant ingredients. In Germany and Europe, compliance with these limits is controlled not only by the monitoring authorities but also by the manufacturers. You can see this when products are recalled, for example, when increased levels of certain alkaloids are given as the reason. However, with the huge variety of naturally occurring substances, you have to rely on the history of consumption of the foods, since it is impossible to analyse every single substance.

History of consumption – what exactly does that mean?

This is the wealth of experience regarding the consumption of a food. If no adverse health effects are apparent in this context over a long period of time, this is referred to as a “safe history of consumption”. The situation is different for plants that are known in other parts of the world but are still considered new to us here in Europe. To avoid any unpleasant surprises, anything that was not consumed to a significant extent in the EU before 1997 must undergo a type of authorisation procedure with risk assessment as a “novel food” before being placed on the market.

Are there any trends that stand out to you?

Our work focused on pyrrolizidine alkaloids for a long time. It has now been possible to reduce their concentrations in many foods and there are maximum levels for various foods. This is also a credit to the BfR. In our opinion, it is critical that high-dose plant extracts are increasingly available, but not much is actually known about their health effects and it is therefore difficult to assess whether they pose a risk. It is also interesting that the public perception of the risk posed by natural toxins is not particularly high and that many plant toxins are largely unknown. One example is phasin, which is found in raw beans: beans should not be eaten raw, they should be cooked for a sufficiently long time to avoid poisoning. Phasin glues red blood cells together. Above a certain dose, consumption can lead to gastrointestinal problems with vomiting and diarrhoea and, in extreme cases, death if large quantities are consumed.

What can consumers do?

When it comes to nutrition, the BfR generally recommends variety and diversity. This avoids one-sided exposure to potentially harmful substances, the presence of which must always be expected. A varied diet also ensures a complete supply of various nutrients. —



© BfR

**“Sometimes only
the dose makes the
difference to health.”**

**DR BENJAMIN SACHSE,
BFR TOXICOLOGIST**



KEEP YOUR HANDS OFF THE PAINT?

Aniline may be present in children's finger paint as an impurity, residue or degradation product. One possible source may be the dyes for which aniline is used in the production. Since aniline can damage the nervous system and the red blood cells, and can possibly lead to allergies (contact dermatitis), their presence in finger paint is restricted. According to research carried out by the BfR, the limit of 10 mg of free aniline per kilogramme of finger paint is complied with; to date, state chemical investigations offices have not had to object to aniline levels in finger paint above the legal limit. Furthermore, the BfR's health risk assessment also shows that negative health consequences for children are unlikely, even if the limit is fully exploited.

More information



BfR opinion
"Aniline in finger paints"
(pdf)

Please no **MOAH**

Mineral oil components can be contained in packaging, such as jute bags or cardboard boxes made from recycled waste paper, and can be transferred from these to food. Does this pose any health risks? According to the European Food Safety Authority (EFSA), based on current knowledge, no adverse health effects are to be expected from the current intake levels of saturated hydrocarbons – MOSH for short – via food. However, some aromatic hydrocarbons (MOAH) may cause cancer and, therefore, pose a health concern according to EFSA. The BfR recommends reducing mineral oil contamination as much as possible, for example, by using virgin fibre cardboard boxes, mineral oil-free printing inks or functional barriers between food and packaging.

More information

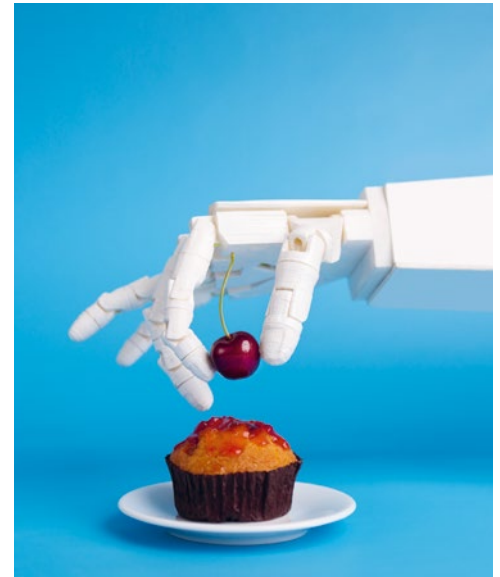


BfR communication
"New EFSA risk
assessment: mineral
oil residues in food"
(pdf)



AI detects food trends

The “BfR Weak Signal Miner” aims to detect new nutritional trends with potentially undesirable health consequences for consumers. The computer program analyses large volumes of text and publication data, including from social media, for trends in the food and feed sector. It is being developed at the BfR as part of the HOLiFOOD project funded by the European Union with participants from several EU countries. HOLiFOOD will run until October 2026 with the aim of improving risk analysis in food safety in Europe. Artificial intelligence and big data technologies will support early warning and forecasting systems for emerging health risks.



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Micronutrients and Co.

Which foods are good sources of iron or vitamin C? Why does my body need minerals? Do I need food supplements to stay healthy? The BfR answers these and other questions on its new internet portal “Mikronährstoffe und Co.” (Micronutrients and Co.). Consumers will find useful information here on vitamins, minerals and other substances that are often added to food supplements or conventional foods. Risk assessment opinions elaborated by the BfR and the BfR’s proposals for maximum levels for vitamins and minerals in food supplements and fortified foods are also part of the new portal.

More information



BfR portal
“Micronutrients and Co.”

More information



Project website
“Holifood”

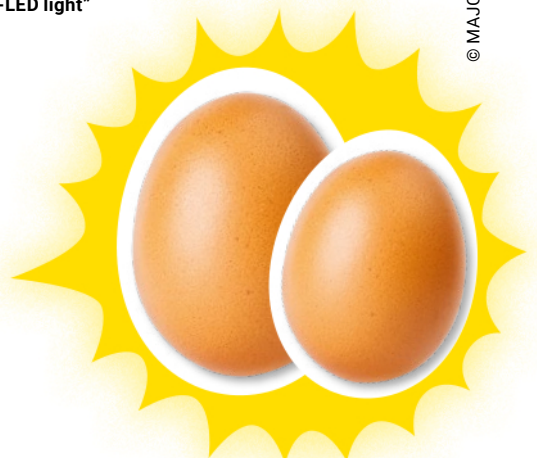
“Light therapy” for eggs

Pathogens, such as *Salmonella* and *Campylobacter*, can lurk on raw eggs. These bacteria can cause food-borne infections along with stomach cramps, diarrhoea and vomiting. In extreme cases, these kinds of infections can be life-threatening for people with a weakened or not yet fully developed immune system. A BfR research project funded by the BMEL shows that UV-C LED light reduces the number of bacteria on eggs if they are not or only slightly stained. The ultraviolet radiation, which is invisible to the human eye, damages the microorganisms, killing them.

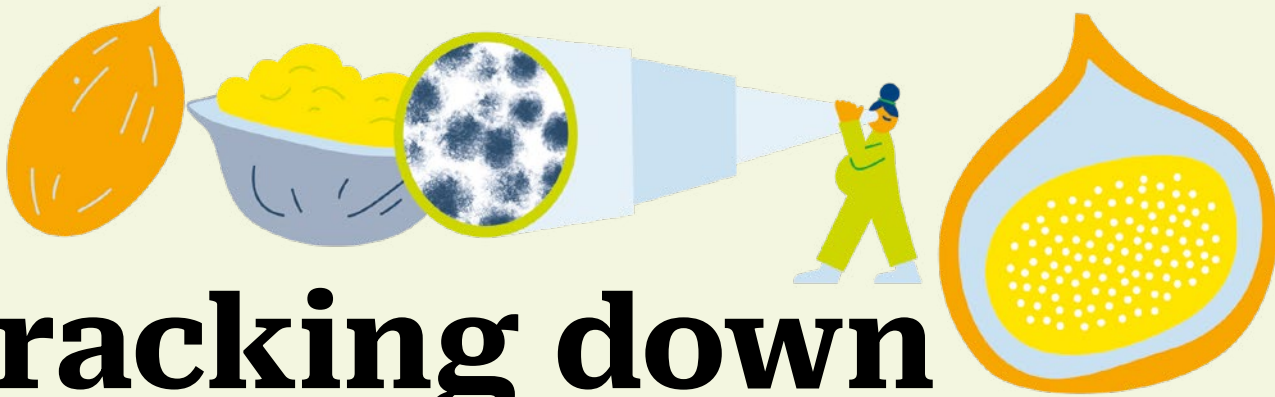
More information



BfR opinion
“Treating eggs with
UV-C-LED light”
(pdf)



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Tracking down mould toxins

Harmful mould toxins are mainly found in plant-based foods. However, the latest data shows that they may also be lurking in cheese and meat.

Illustrations: Susann Stefanizen





Whether stored incorrectly or simply forgotten – many people have certainly experienced an unpleasant surprise due to mouldy food. Mould is hard to miss but mould toxins are real masters of camouflage. The toxins, known in science as mycotoxins, are formed as secondary metabolites in various genera of mould. They can be harmful to health if ingested with food. One example of these toxic substances are aflatoxins, which are produced by moulds of the genera *Aspergillus flavus* and *Aspergillus parasiticus*. Their main representative – aflatoxin B1 – is one of the strongest toxic and carcinogenic substances found in nature. In Germany and other Central European countries, the risk of acute damage to health, such as liver failure, from ingesting large quantities of aflatoxins from food is very low. Therefore, the effects of long-term ingestion are more relevant when assessing the health risks. These include liver and kidney cancer. Thus, ingestion of these substances should be as

low as possible. Aflatoxins are mostly found in regions with a warm and humid climate. However, it is already apparent that they are also increasingly prevalent in grains in Europe due to climate change.

ODOURLESS, TASTELESS, INVISIBLE

In contrast to moulds, mycotoxins are not visible to the naked eye. They are also odourless and tasteless. They sometimes form while plants are growing in the field or during transport and storage. The toxic substances are mainly found in plant-based foods, such as grains (e.g. maize, wheat) and products made from them, as well as in dried fruit, nuts and dried spices. Some mycotoxins, including aflatoxins, can pass into products derived from livestock, such as milk, via contaminated feed.

Since mycotoxins are toxic substances that are not man-made but of natural origin, their occurrence cannot be completely avoided. For this reason, the European Commission has set maximum levels for various mycotoxins, such as aflatoxins, in individual foods and in some feeds. Food companies have to ensure that the legal maximum levels are not exceeded in their products. In addition to their own monitoring, products are randomly checked by German federal states' ("Laender") relevant monitoring authorities. EU-wide maximum levels for mycotoxins are currently

TIPS

For avoiding mould altogether:

Avoid hoarding: buy food as fresh as possible, store in a clean, dry and cool place and consume in good time.

Remove bread crumbs from surfaces and chopping boards.

Clean bread bins and similar items once a week and wipe down with diluted vinegar.

What should you do with food that is already mouldy?

Do not eat mouldy food – throw it away immediately, as mould is “contagious”.

Food should also be thrown away completely if there are spots of mould, such as on loaves of bread.

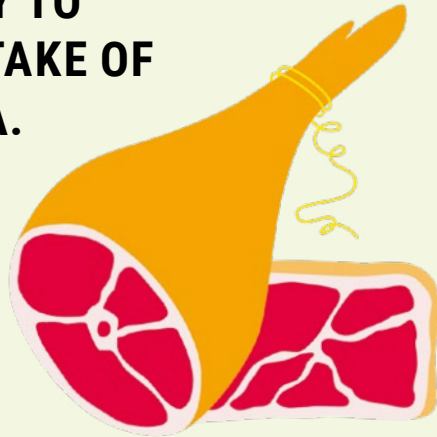
Mould-ripened cheeses, such as Roquefort and Camembert, are harmless; these kinds of cheese should always be stored in separate packaging to distinguish it from “real” mould.

More information



BfR leaflet
“Protection against mould
toxins in food” (pdf) (in German)

THE CONSUMPTION OF PRESERVED MEAT, SUCH AS CURED HAM, CAN CONTRIBUTE SIGNIFICANTLY TO THE TOTAL INTAKE OF OCHRATOXIN A.



only exceeded in individual cases. With regard to aflatoxins, pistachios, dried fruit and dried spices produced outside the European Union in particular may contain levels above the maximum limit.

MATURED CHEESE AND HAM ALSO AFFECTED

Ochratoxin A is a mould toxin that is much more prevalent in Europe. If ingested over a long period of time, it can lead to kidney damage in humans. Carcinogenic effects on the kidneys have also been observed in animal experiments. Ochratoxin A has also mainly been detected in plant-based foods, including grains, coffee, cocoa, wine, liquorice and dried fruits, such as dates and figs. In 2020, the European Food Safety Authority (EFSA) published a new report on this issue. The result: in addition to plant-based foods, ochratoxin A was also detected in a small number of matured hard cheese samples – mostly on or near the rind of “Parmigiano Reggiano” and “Grana Padano” – and in cured ham. Both cases concern traditionally manufactured products with a long maturing period.

Scientists at the German Federal Institute for Risk Assessment (BfR) have developed an analytical method for determining the toxic substance ochratoxin A in cheese. This was made available

to the official control laboratories as a tool for a national monitoring programme for ochratoxin A in hard cheese and blue cheese. Carried out in 2023, the evaluation of the results is currently still pending. Initial preliminary investigations carried out by the BfR on ochratoxin A in matured hard cheese on the German market show that some samples contain the mould toxin. The differences between grated cheese, cheese in the form of flakes or in a block were particularly striking: the grated samples showed higher concentrations of ochratoxin A than the other two product forms. This is probably because manufacturers are allowed to process up to 18 % of the rind in the grated product form.

Further studies carried out by the BfR on ochratoxin A concentrations in dried and cured ham confirm the EFSA's statement that the consumption of preserved meat, for example, cured ham varieties like Serrano and Parma ham, can contribute significantly to the total intake of ochratoxin A. "The findings show that mycotoxins can also occur in foods of animal origin without transfer from feed. This is an aspect that has barely been considered so far," says chemist Dr Stefan Weigel, who investigates plant toxins and mycotoxins at the BfR. "Long maturing periods and special presentation forms could be a significant influencing factor here."



NEW TRACES OF UNKNOWN MOULD TOXINS

It is assumed that in addition to the hundreds of known mycotoxins, a large number of previously undiscovered mould toxins are present in the environment. Weigel and his team at the BfR have developed methods that also detect previously unknown mycotoxin compounds so that as many mycotoxins as possible can be measured at the same time in one sample. Other mould toxins and previously unknown transformation products of mould toxins can also be determined in addition to the mycotoxins for which there are presently routine tests. "In the next step, it's important to find out how the previously unknown substances affect human health," says Weigel. —

More information



BfR information
"Mycotoxins"

ALSO IMPORTANT TO KNOW:

Mycotoxins are resistant to heat and cold. They cannot be destroyed by cooking, baking, frying or freezing.

Children, pregnant women and people with a weakened immune system are particularly sensitive to the possible harmful effects of mycotoxins.



GENE CUTTING



New bio-
technological
methods
allow precise
interventions in
genetic material
– how well can
changes be
detected?

No plant breeding without mutation. Mutagenesis – the creation of genetic changes – is the beginning of new fruit and vegetable varieties, of higher-yield maize or tastier apples. In conventional breeding, plants are irradiated or chemically treated to accelerate the occurrence of mutations. It has become possible to change genetic material in a targeted way with the development of plant biotechnology. Accident becomes intention.

New methods such as the CRISPR/Cas9 “gene scissors” now allow the smallest of interventions. The result is indistinguishable from natural mutations; in a sense, nano-surgery on the genetic information of wheat, rapeseed, etc. Is public opinion changing?

Hermann Broll is not willing to give a statement, no matter how much we would like to know. The biologist at the German Federal Institute for Risk Assessment (BfR) keeps his distance from all opinions and intentions in this field and concentrates solely on the scientific facts. Broll is an expert in genetic analyses. He was involved at an early stage in work on how to detect genetic information from genetically modified organisms (GMOs) in food and feed.

FAST COPIER FOR GENETIC MATERIAL

“The methods established by my colleagues and I at the BfR’s predecessor – the German Federal Institute for Consumer Health Protection and Veterinary Medicine – were the first standard worldwide,” Broll recalls. They are based on the polymerase chain reaction (PCR). PCR is a kind of fast copier for DNA genetic information. It makes it possible to detect

even the smallest traces of a specific genetic material sequence in food.

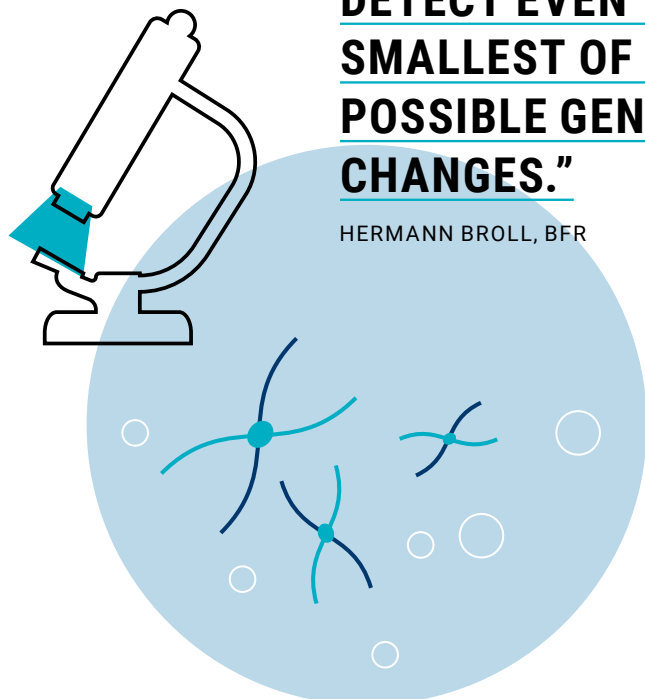
In 2008, Hermann Broll organised the first major international conference on the detection of GMOs together with the European Commission’s Joint Research Centre (EC-JRC). A lot has happened since then. New methods like gene scissors have revolutionised biotechnology, new analytical methods make it possible to decipher entire genomes (the complete genetic information) and make it easier to detect GMOs. Reason enough for Broll to bring the scientific community together again: in March 2023, almost 500 participants from 55 countries met in Berlin for a conference on GMO analysis and new genomic techniques.

EVEN THE SMALLEST CHANGES DETECTABLE

An important topic of discussion were GMOs, in which only a single base in the genetic information DNA is replaced using gene scissors. This corresponds to one letter in a book with tens of thousands of pages. The technical term for this is point mutation. “In principle, it is possible to detect even this smallest of all possible genetic changes,” says Broll. “However, most conference participants agreed that it is not yet possible to determine who caused this change, in other words, how the change came about.” Whether of natural or artificial origin, intentional or accidental – the mutation does not reveal its origin.

“IN PRINCIPLE, IT IS POSSIBLE TO DETECT EVEN THE SMALLEST OF ALL POSSIBLE GENETIC CHANGES.”

HERMANN BROLL, BFR



Are gene scissors (which are also expanding into medicine) and other “new genomic techniques” still genetic engineering in the conventional sense? In 2018, the European Court of Justice ruled that plants and animals modified using new genomic techniques are GMOs. However, this did not put an end to the discussion, which has only really just begun. For example, how risky are genetically modified plants, where the genetic



“IT HAS BECOME CLEAR HOW BIG THE DIFFERENCES ARE IN THE LABORATORIES. EUROPE AND NORTH AMERICA ARE WELL EQUIPPED FOR DETECTING GMOS, WHEREAS THIS IS OFTEN NOT THE CASE IN ASIA AND AFRICA.”

material cannot be distinguished from that of conventional breeds? What about being labelled “genetically modified”, what about traceability?

DISCUSSION ABOUT EASING RESTRICTIONS

With this in mind, the European Commission is making efforts to rethink the current legal situation and adapt it to the new methods. The intention is to ease the current restrictions for plants that have been produced using new genomic techniques, such as CRISPR/Cas9, and that only contain genetic material that is also present in the species’ current gene pool. This affects things such as labelling as “genetic engineering” and the approval procedure. Whether or not EU will follow the suggestions is still unknown (as of September 2023).

Hermann Broll also mentions a second result of the Berlin conference that has very practical significance: “It has once again become clear how big the differences are in the laboratories. Europe and North America are well equipped for detecting GMOs, whereas this is often not the case in Asia and Africa.” From Broll’s perspective, this needs to be remedied. For example, if an African country wants to export “genetically modified-free food” to Europe, it must be able to prove this. This also means that European decisions on plant biotechnology reach far beyond the continent. Even if it does only concern point mutations. —

More information



Broll, H. et al. 2019. **European Court of Justice decision for genome editing: Consequences on food/feed risk assessment and detection.** Food Control, Volume 104, 288-291, DOI: 10.1016/j.foodcont.2019.05.002



Video recordings of the talks **International Conference on GMO Analysis and New Genomic Techniques 2023**

Goodbye, allergies?

Special infant formula products claim to protect infants from allergies. However, their benefit has not been proven.

The most natural and healthiest nutrition for infants is breastfeeding. There is a wide range of industrially produced infant formula products for infants who are not or not fully breastfed. These include products labelled as "HA". They contain partially hydrolysed protein – in other words, protein that has been broken down into smaller components through a special processing technology. Some manufacturers claim that such products are particularly well tolerated and suitable for allergy prevention in infants at high risk of allergies. However, there has been a controversial debate in recent years as to whether these products really offer such benefits. The German Federal Institute for Risk Assessment (BfR) has investigated this issue.

It is known that infants with a genetic predisposition – when the parents or direct siblings are affected by an allergy – have an increased risk of allergic diseases. It is thus understandable that parents want their children to be protected from this.

Until recently, it was recommended that infants at increased risk of allergies who are not or not fully breastfed, should be fed a partially hydrolysed infant formula until complementary feeding is started. This recommendation was based on the assumption that the risk of allergies is reduced if only small amounts of intact cow's milk protein, i. e. protein that has not been broken down, are consumed in the first few months of life.

DISPUTED STUDY

In Germany, this recommendation was mainly based on the "GINI Study" (The German Infant Nutritional

Intervention Study). This study investigated the efficacy of different hydrolysed infant formulas in preventing allergies in infants born between 1995 and 1998. The study reported for one of the products a protective effect on the risk of atopic dermatitis. However, in the view of the BfR, methodological shortcomings of the study limit the reliability of the results. Regardless of this, the products studied are no longer available in their original composition.

The benefits of such infant formulas has therefore been subject of an increasing debate. The assessment is complicated by differences in study design and product characteristics, for example, due to variation in protein hydrolysates obtained from different manufacturing processes. It is acknowledged that infant formula products currently available on the market are suitable for infants from a nutritional point of view; however, their effectiveness in preventing allergies is questionable. —

INFANT FORMULA CONSUMPTION IN GERMANY (KIESEL STUDY 2014–2017)

73 %
of children aged between 0.5 and 5 years have received infant formula at some point

24 %
of children aged between 0.5 and 5 years have been given HA infant formula

FOLIC ACID

FOLATE

Folic acid is the synthetic form of a vitamin that was originally identified in green, leafy vegetables: folate (lat. *folium* for leaf). Foliates, which occur naturally in food, are essential for humans. A factsheet.

Why do we need folic acid/folate?

The body converts folic acid and folates into the active form tetrahydrofolate. This is how folate becomes biologically active in many metabolic processes, especially in the synthesis of DNA. Thereby it is also important for cell division and growth.

LAMB'S LETTUCE

146

DEEP-FROZEN GREEN PEAS, COOKED

78

STRAWBERRIES

44

OAT FLAKES

87

LEAF SPINACH, COOKED

105

THIS MUCH FOLATE CAN BE FOUND IN ...

in micrograms (μg) per 100 grams (g)

143

CAMEMBERT

COW'S MILK

9

26

BROCCOLI, STEAMED

22

ORANGE

34

RYE WHOLEMEAL/RYE AND WHEAT BREAD

58

HEN'S EGG, BOILED



Other folate sources: tomatoes, nuts and seeds.

Foliates are water-soluble and sensitive to light and heat. Therefore, prepare foods carefully.

With a balanced diet made up of plenty of green vegetables, pulses and wholemeal products, healthy people do not need vitamin pills or special fortified foods to meet their folate requirements. Food supplements can help if an insufficient folate supply has been detected. However, they should not contain more than 200 µg of folic acid per daily dose. Folic acid intakes of more than 1,000 µg per day increase the risk of adverse health effects, such as the masking of symptoms of a vitamin B12 deficiency.

Maximum level recommended by the BfR

per daily dose of a food supplement:



There are numerous foods fortified with folic acid: examples in Germany include table salt, soft drinks, breakfast cereals and dairy products.



How much folate (in folate equivalents*)? per day

300 µg

ADOLESCENTS AND ADULTS

550 µg

PREGNANT WOMEN

450 µg

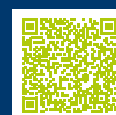
BREASTFEEDING WOMEN

Women planning to have children and those in their first trimester of pregnancy should take a supplement containing 400 µg folic acid per day in addition to consuming 550 µg of food folates via their diet. This reduces the risk of birth defects in the child (for example, neural tube defects such as *spina bifida*).

* Folic acid and folates are absorbed and metabolised differently by the body. The amounts of folic acid and folate are specified as folate equivalents to account for different bioavailability.



More information

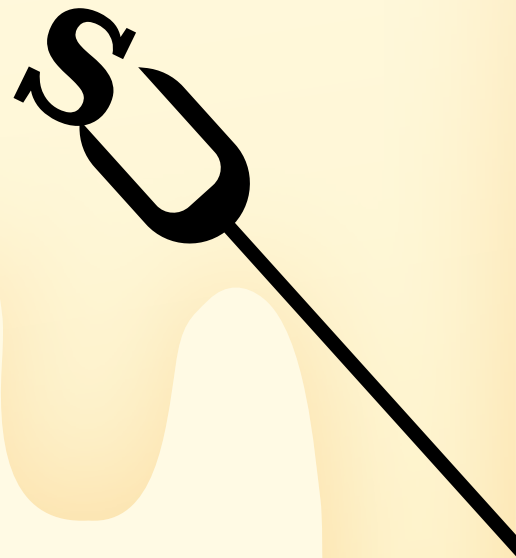


BfR FAQ
"Folate and folic acid"

SOCIABLE, ENJOYABLE, DANGEROUS



Winter is fondue and raclette season. However, this cosy feast can end in an unpleasant foodborne infection. What should you look out for?



Little pieces of meat and vegetables from the raclette pan or fondue fork are a popular way to warm up on the inside when it is cold outside. However, pathogens that may be present on raw meat may be transferred to food during the preparation and cooking of the ingredients, which are then eaten without further heating. For example, if ingredients are on the same plate or come into contact with the same cutlery.

Campylobacter bacteria are particularly common on raw poultry. *Campylobacter* infection is the most frequently reported bacterial foodborne disease in Germany and the European Union. A total of 43,166 cases were reported in Germany in 2022. Young children and young adults are particularly susceptible to infection. Even small quantities of germs suffice. This results in diarrhoea with fever and stomach cramps, which usually go away on their own after a few days. However, in individual cases severe nerve disorders or joint inflammation are also possible.

On the one hand, infections with *Campylobacter* germs occur more frequently in the summer months. Transmission by insects leads to more frequent colonisation of the

germ in animal populations. As a result, *Campylobacter* are increasingly found on raw poultry. On the other hand, there is also an annual short-term surge in the number of cases at the beginning of the year. In a study, the Robert Koch Institute (RKI) was able to show a connection between *Campylobacter* enteritis cases after Christmas and New Year's Eve and meat fondue or raclette meals during the holidays, particularly when chicken was on the menu.

GOOD KITCHEN HYGIENE IS ESSENTIAL

Good hygiene when handling raw animal foods is essential in avoiding infections with *Campylobacter*. This applies to preparation in the kitchen as well as at the dining table itself, when family and friends gather around the raclette dish or fondue pot. It is important that there is no spread of germs, i.e., cross-contamination. This is the term

SEPARATE AND CLEAN – TO AVOID A BAD ENDING.

usually used to describe the transfer of germs from raw food to other food. This can happen if they come into direct contact with each other. However, indirect transmission via hands, work surfaces, cutlery or other kitchen utensils is also possible. For example, bacteria can pass from uncooked meat to cooked pieces, potatoes or vegetable pieces if the fork or plate is not changed. Raw meat, especially poultry, and food that is consumed without further heating should therefore be strictly separated. Good kitchen hygiene also includes thoroughly cleaning hands, kitchen utensils and preparation surfaces after contact with raw food of animal origin and before preparing other foods or elements of a meal.

HEAT-SENSITIVE MASTERS OF CAMOUFLAGE

Since *Campylobacter* germs do not cause food spoilage, it is not possible to detect their presence by appearance or smell. However, like most foodborne pathogens, *Campylobacter* can be killed by heating: a temperature of 70 °C must be reached in the centre of the food for at least two minutes.

Regardless of this, “separate and clean” is way to go for fondue and raclette ingredients, cutlery and more. This ensures avoiding a bad ending. —

More information



BfR-FAQ
„Protection against foodborne
infections in private households”
(pdf)

“Science is actually completely neutral”

Priority for facts: physicist, comedian and author (“Lichtblick statt Blackout” – Ray of hope instead of a blackout) Vince Ebert calls for the separation of science and ideology – and more courage to take risks.

Vince Ebert, what do you think about risk?

I find it astonishing that we humans either completely overestimate or underestimate risks. We are afraid of shark attacks, terrorist attacks and glyphosate – low risk. And at the same time, we smoke and ride motorbikes, even get married – high risk. When dealing with risks, we let our gut feeling guide us instead of looking at figures and statistics. It's like: my gut feeling tells me that's how it is, so it must be true.

Can we do anything to avoid that?

Knowledge of science and maths helps us to better assess risks, because you learn to deal with numbers and do the calculations. In maths lessons, real-life problems should be used and checked with statistics. Instead of using unrealistic questions, such as: I have a bowl with ten red balls and ten black balls. If I take out two red balls, how does the probability of drawing a red ball in a lottery change?

What is your assessment of how risks are dealt with in Germany?

There is often a zero-risk mentality. If there is a particular source of danger, the idea is that it

should be eliminated completely. For example: the coronavirus pandemic. We wanted to reduce incidences to zero without fail. To do this, all public life was brought to a standstill. But then the economists said: we're destroying the economy! And psychologists said: children will go crazy if we continue with this! We often forget that decisions made to counter risks can create other risks and even make the problem worse. Another example is shutting down our nuclear power plants because we think they are too dangerous. The consequences are other risks, such as energy shortages and possible blackouts. There is simply no ideal solution and no zero risk for many complex issues. It is very difficult to accept that life is a risk.

So we need more courage to take risks?

I lived in the USA for a year, and the way people there deal with mistakes is different. They are more likely to try things out and take more risks. For example, when an app is programmed over there, it often happens quickly and the finished product is not perfect, but the essentials work. Here in Germany, it takes considerably longer because we want it to be perfect. We spend a year fiddling about with a shower fitting or a cylinder head gasket, which then work 120

percent. But when it comes to major social concepts or meeting future challenges, many things are just unpredictable. This is why we have to be more willing to weigh risks against each other and accept that not everything can be planned!

Are we allowed to make jokes about risks?

Definitely! In one of my earlier comedy routines I had a bit that went something like this: “The odds of winning the lottery are 140 million to one – it could be me! The risk of developing lung cancer is one in seven for lifelong smokers – why would I, of all people, get sick?” This joke highlights the irrational way in which we deal with

“It is very difficult to accept that life is a risk.”

VINCE EBERT,
PHYSICIST AND COMEDIAN



© Frank Eidel

statistics and probabilities. I try to use humour to make people understand these correlations. If I can laugh about something, I might become aware of the inconsistency in my own behaviour and give it some thought. At least, that’s what I hope.

Whether the coronavirus pandemic, climate change or assessing risks: science plays a central role in society. How well is it coping?

I emphasise this again and again, even in my routines: science is actually completely neutral. First of all, it only explains the causal relationships between things. It does not say how we as a society should react to these findings. A nuclear physicist can calculate how much energy is released during nuclear fission. But nuclear physics does not tell us whether nuclear energy is good or bad or whether we should use it or not.

Is this still the general perception? Don’t scientists today often act as admonishers and give warnings?

There are prominent climate researchers who clearly see themselves as activists. They want to change something; they want a political and social turnaround. That’s all legitimate. But when they speak as scientists, I expect facts first – and not an assessment. I think that mixing up these roles is a dangerous development that undermines the credibility of science. That also applies to science journalism, by the way. Reporters used to simply explain how a petrol engine or a microwave works, but nowadays, they also include their ideology. I don’t approve. Good science communicators should provide information, but not preach. —

Detecting risky substances

The European PARC project aims to uncover the unknown when it comes to chemicals and bring their risk assessment to a new level.



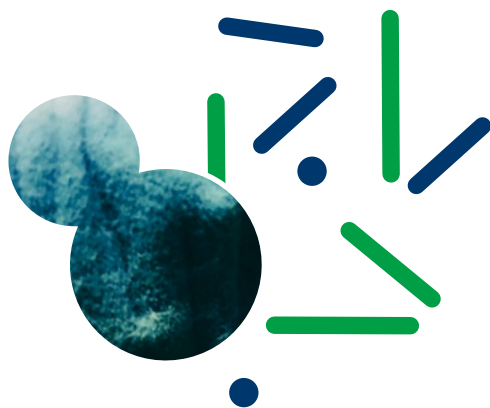
Are you familiar with enniatin B1? Probably not. It is a mould toxin, or mycotoxin to use its scientific name (see also the article on mould toxins on page 18). Enniatin B1 is produced by microscopic parasitic sac fungi *Fusarium*, which is found all around the world. Only experts have been familiar with the substance up to now, but this could change. Mycotoxins belonging to the enniatin group, such as enniatin B1, are being detected more and more frequently by food monitoring organisations thanks to improved analysis methods. These mycotoxins are mainly found in grains, such as wheat, oats, maize, barley, rye, rice and products made from these, and also in nuts and dried fruit.

Just like other mycotoxins, enniatins are used by *Fusarium* to defend against bacteria, other types of fungi, insects and worms. These kinds of “bioweapons” can lead to undesirable health effects in humans. Some studies on enniatins point towards effects that are carcinogenic, mutagenic, that compromise the immune system and that damage the liver, nerves and fertility.

The astonishing thing: knowledge about enniatins is still incomplete despite their widespread prevalence and sometimes high concentration in food and feed. This is insufficient for assessing the health risk.

“The mould toxin enniatin B1 is widespread, but knowledge of its toxic effects is incomplete. We are changing that.”

DR JESSICA DIETRICH, BFR



However, this may soon change because an international research team involving the German Federal Institute for Risk Assessment (BfR) is addressing the issue. “Our aim is to study the hazard potential of enniatin B1 and similar compounds, therefore improving the still incomplete data on the toxic effects,” says Dr Jessica Dietrich. The food chemist is supervising the project as part of an extensive European research project called PARC (“Partnership for the Assessment of Risks from Chemicals”).

200 PARTNERS AGAINST CHEMICAL RISKS

The PARC project, which began 2022 and will run for seven years with 200 participants from 29 countries, has a budget of 400 million euros and aims to do nothing less than open up new horizons for the risk assessment of chemicals. Half of the costs are covered by Horizon Europe, the EU’s framework programme for research and innovation. The other half is financed by the respective project participants.

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“A major obstacle to researching mycotoxins like enniatin B1 and similar compounds is the procurement costs,” says Dr Jessica Dietrich. “One thousandth of a gram of a substance can cost as much as 1,000 euros.” It is now possible to overcome this obstacle thanks to the PARC budget. As part of the PARC sub-project on mould toxins, Dietrich and her team are cooperating with a working group at TU Berlin, which chemically synthesises the enniatins’ complicated ring molecules, therefore replacing the time-consuming extraction from the moulds.

The initial plan is to test enniatin B1 and similarly structured compounds in bacterial and cell cultures for possible toxic effects. In addition to closing knowledge gaps, this is another of the BfR’s supporting contribution to PARC: the development of new, animal-free methods. These include, for example, computer models, biochemical analyses of cell processes and experiments on cell cultures and miniature organs (“organoids”). The aim is to reduce animal experiments and to improve health protection for humans.

“New, animal-free methods are used to study mould toxins.”



© BfR

ASSESSING RISKS, REGULATING SUBSTANCES

“An important guiding principle of our project is the practical benefit,” says biochemist Dr Philip Marx-Stölting, who is responsible for coordinating the “hazard assessment” PARC sub-project at the BfR. “Recognising hazards, assessing risks and ultimately regulating them, for example, through policy and authorities, go hand in hand in the PARC project.”

As part of the sub-project, the BfR is also dedicating itself to the task of integrating knowledge from the other segments. It is a bit like putting together pieces of a jigsaw puzzle to make a whole picture. What does a chemical substance change in a cell, an organ or an organism? Is it possible to estimate how a substance affects a person? Can predictions be made for similar chemical compounds?

COOPERATION FOR RAPID PROGRESS

From Marx-Stölting’s perspective, international cooperation plays a decisive role in answering many questions. There are also very practical reasons for this. For example, the guidelines of the Organisation for Economic Co-operation and Development (OECD) stipulate that a test procedure must be recognised by every member country.

The advantage: a test conducted by a method approved by the OECD only needs to be performed in one country. On the other hand, the test procedure itself must first be approved by each OECD country. “You have to have all countries on board for a new testing guideline,” explains Marx-Stölting. “This regulation saves on testing, but at the same time it makes changes long-winded, which is why it’s so important that we work together at an early stage, first in the EU and then internationally.”

The team working on enniatin B1 and other mycotoxins is also international. It includes scientists from Germany and Austria, Norway, Portugal, France, Spain, Slovenia, Belgium and the Netherlands. It looks as though some of the fungi in PARC will soon have to reveal their secrets. —

More information



Marx-Stoelting, P. et al. 2023. **A walk in the PARC: developing and implementing 21st century chemical risk assessment in Europe.** Arch Toxicol 97, 893-908. DOI: 10.1007/s00204-022-03435-7



The BfR is involved in many PARC projects - more information can be found on the project website: „PARC“

Body decoration

under the skin

... and from there even further? Studies carried out by the BfR show for the first time how tattoo ink ingredients are distributed in the body.

At any rate, it is sometimes more, sometimes less complex to find out what tattoo ink consists of through laboratory analyses. Some ingredients are already known to irritate the skin or trigger other undesirable reactions in the body. However, more information is needed to be able to fully assess tattoo inks' health risks: which ingredient ends up in the body and in what quantity? And what happens to it there? There has been no reliable data on this – until now. A team of scientists at the German Federal Institute for Risk Assessment (BfR) has now tracked where tattoo inks go in the body for the first time.

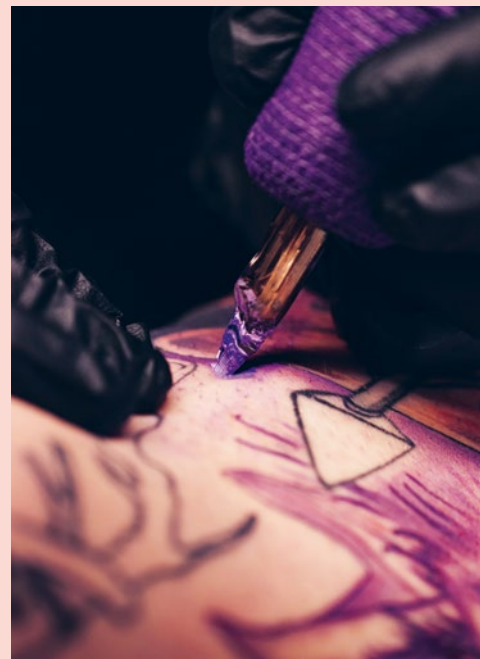
TATTOOING FOR SCIENCE

"For our study, we looked for a total of 24 volunteers who already had at least one tattoo and wanted another one," explains Dr Ines Schreiber, one of the heads of the BfR's Dermatotoxicology Study Centre. After a preliminary interview and examination, they were given

the tattoo of their choice by a professional tattoo artist under laboratory conditions on the premises of the Charité hospital in Berlin.

The study participants gave urine and blood samples shortly before the tattoo needle was applied and at certain intervals during and after the session. It was possible to trace exactly how the liquid components from the tattoo ink enter the blood and are processed by the body's own metabolism using "tracer substances".

"The actual colour pigments remain predominantly in the skin – unlike many of the other ingredients," explains Schreiber. Therefore, her team concentrated on the liquid components of the inks. And these were already detectable in the first blood sample taken shortly after tattooing began. How quickly the substances were metabolised in the body and excreted in the urine was different for each marker substance.



© cloutier-benjamin / Unsplash

One substance was no longer detectable in the urine after around four hours, while others took longer. The data will be used to develop computer models that can predict the time required for metabolisation of other substances in tattoo inks, among other things.

The study also recorded exactly how much colour was used in each case. To do this, the colour bottles were precisely weighed before and after the session. "And then we collected all the needles, cloths and gloves and looked at how much colour was stuck to them," explains Schreiber. The surprising thing: on average, around a fifth of the colour used actually ends up under the skin. The results of the study will make it possible to assess and evaluate the health risks of tattooing more accurately in future. For Ines Schreiber, the effort was definitely worth it: "Now we have the most realistic data that we could possibly have." —

Collecting data, saving lives

Poisoning accidents have yet not been systematically recorded throughout Germany. Children in particular can suffer serious damage. The BfR is therefore setting up a national poisoning register.



A frightening scenario for many parents: distracted for just a moment, the child nibbles on some berries or leaves from a poisonous plant or takes a sip of a cleaning product that wasn't properly sealed. "Fortunately, most poisoning accidents end relatively mildly," says Kathrin Begemann. "However, poisoning can also cause serious permanent damage or, in the worst case, even be fatal – especially if it is not treated quickly enough." The pharmacist has been researching the poisoning potential of both chemicals and plants at the German Federal Institute

for Risk Assessment (BfR) for decades. Examples include the poisonous doppelgangers of wild garlic and edible mushrooms.

If family members or childcare staff in nurseries and schools find themselves in such a situation, the federal states' poison centres should be the first port of call. Staffed around the clock, the experts at the other end of the line provide immediate information on first aid and further treatment in the event of suspected poisoning. They also advise the emergency services or medical

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© BfR

staff treating poisoning incidents. Poison centres throughout Germany receive around 250,000 calls a year.

BFR HAS BEEN COLLECTING DATA FOR SOME TIME

Poisoning accidents have yet not been systematically recorded throughout Germany. That is going to change: the BfR is setting up a national poisoning register. This is where the anonymised data on all poisoning accidents will come together. The BfR and its predecessor institutions have been collecting case reports on poisonings since 1990. The German Chemicals Act is the basis for this. According to this law, doctors must report all cases of poisoning with chemicals to the BfR, including suspected cases.

However, this has worked less well in practice so far. In fact, only up to two percent of current poisoning reports come from doctors' surgeries and hospitals. The majority of reports originate from employers' liability insurance associations and other statutory accident insurance companies, for example, on accidents at work involving chemicals.

The new national poisoning register aims to merge and evaluate this data with the information from calls to the poison centres in future. In addition to the substance responsible for the poisoning, the associated product and the type of ingestion will also be recorded, for example, whether the substance was swallowed or inhaled. The age group and gender of the person affected are also recorded. Instead of the approximately 8,000 reports that are received in the case database under the German Chemi-

POISONING ACCIDENTS AMONG CHILDREN

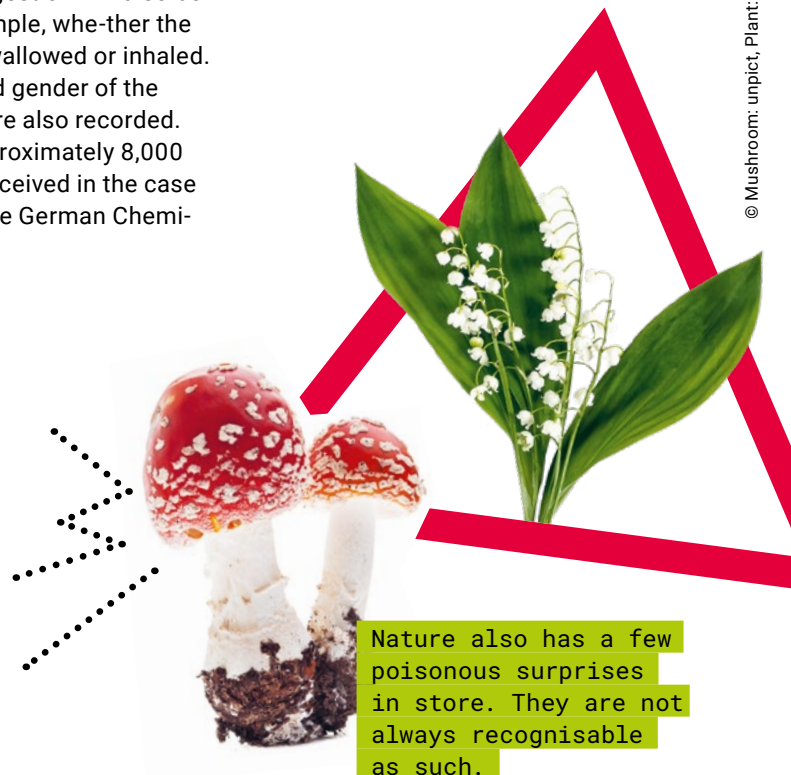
The BfR has developed a smart-phone app for poisoning accidents among children as a practical information and reference tool. You can call a poison centre for your federal state directly from the app in an emergency. There is also information on particular hazards in the home and advice on preventing poisoning accidents. To install the app, scan the relevant QR code or search for "Vergiftungsunfälle bei Kindern" in the app store.



App for Android
(in German)



App for iOS
(in German)



Nature also has a few poisonous surprises in store. They are not always recognisable as such.

Potentially dangerous products should be recognised more quickly and the risk of further poisoning accidents should be reduced.

ALPHANUMERIC LIFESAVER

Poison centres need the most precise information possible on the product in question in the event of a poisoning incident. Since the beginning of 2021, more and more household chemicals, such as cleaning products, have been labelled with the EU-wide standardised “UFI code”. The abbreviation stands for “unique formula identifier”. This 16-digit code consisting of numbers and letters allows poison centres to quickly and clearly identify the requested product and its ingredients. Specific information on the correct treatment can be provided based on the exact composition.

calcs Act on average each year at the moment, this figure is expected to rise to around 190,000 cases in the future. However, poisonings with narcotics and alcoholic beverages will not be recorded, since their effects are already known; neither will poisonings with medicines, as a separate monitoring system for medicines already exists.

RECOGNISING DANGEROUS PRODUCTS FASTER

“The aim is to obtain a better overview of the actual number of poisoning accidents in Germany,” explains Dr Nina Glaser, who is coordinating and

preparing the introduction of the poisoning register at the BfR together with Kathrin Begemann. This will make it possible to recognise potentially dangerous products more quickly and reduce the risk of further poisoning accidents. “For example, by providing the packaging with a child-resistant cap or by the relevant monitoring authorities sometimes taking a product off the market completely.”

The idea of a national poisoning register has been around for some time. The BfR Committee for the Assessment of Intoxications proposed this kind of register back in 2014. At the beginning of 2018, its introduction was formalised in an agreement between the then “Grand Coalition” government of the CDU/CSU and SPD. Preparations have been underway since then. After all, data from different sources has to be merged and processed. The plan is for the register to be launched at the beginning of 2026 – and, in the best case, save lives with fast and accurate information on poisoning incidents. —



More information



BfR information
“Poisoning”

Gene on, gene off

Environmental influences can activate genes. However, there are no detection methods as yet. A research team at the BfR wants to change this.

Does our lifestyle change our genes? Are they influenced by ingredients in food, cosmetics, textiles or packaging? Clarifying this question would be a milestone in health risk assessment. This will require test methods to identify what are known as epigenetically active substances. They can switch on deactivated genes or put activated genes into sleep mode. Dr Josephine Kugler is investigating detection methods at the German Federal Institute for Risk Assessment (BfR). The biochemist wants to develop molecular, animal-free tools that can detect cell changes caused by epigenetically active substances.

FOLDED, PACKAGED AND COILED

Each of our cells contains two metre-long DNA strands with different base sequences that are tightly folded and coiled in a tiny space. The genes' coiling determines the cell type, i.e. heart, skin or nerve cell, and also influences the behaviour of the cells, such as the division rate. "Some genes are packaged so well by this coiling and the closely aligned DNA sequences that they are inaccessible and inactive," explains Kugler.

The DNA strands are coiled around histones. These are proteins that package the DNA in the cells. "Histones have small rods that stick out of the coiled DNA, like clips on hair curlers," explains Kugler. Substances from the environment or hormones that are released due to anxiety or happiness can stimulate or change the histone rods and activate or deactivate the packaged genes. "Two people can therefore have the same cancer gene, but it could be that only one of them actually develops cancer."

Dr Josephine Kugler works on epigenetically active substances at the BfR.



Kugler and her team work with cultured human breast cancer cells to detect the epigenetic effects of substances. These work well because they grow quickly. Students from the "Life Science" department of the Berlin University of Applied Sciences are also providing support as part of a cooperation agreement. The team is simulating the processes triggered by epigenetically active substances in the laboratory to develop a test method. The breast cancer cells are labelled with easily detectable epigenetic markers. Then they wait. Changes in the histones can only be observed under the microscope after several hours. With plenty of patience, the researchers are laying the foundations for a test procedure that could make an important contribution to the risk assessment of chemicals in the future. —

EPIGENETICS

Epigenetics is a young field of research in molecular biology. The prefix "epi" comes from the Greek and means "over". Epigenetics deals with the mechanisms that control the accessibility of genes and ultimately their activity. It is assumed that the state of our genes changes over our lifetime. Both activated and deactivated genes can contribute to the onset of diseases. This would also explain why identical twins with identical genes can develop different diseases over their lifetimes.

ENTERING

Eternal companions at the end of the road:
the possible end of PFAS chemicals.

THE FINAL PHASE

Takeaway cups, non-stick pans and outdoor clothing are products that could not be more different at first glance. Only on closer inspection do they reveal what they have in common: they repel water, grease and dirt. This is due to the per- and polyfluoroalkyl substances – PFAS for short. The group of these industrially produced chemicals comprises more than 10,000 substances. However, the positive material properties contrast with the negative impacts on humans, animals and nature. PFAS spread easily in the environment and remain in water, soil, plants and living organisms for a long time. They have now been detected all around the world, even in drinking water and in the food chain. The German Federal Institute for Risk Assessment (BfR) estimates that the total intake of alarming PFAS

in around half of the adult population in Germany is above the level at which adverse health effects are not to be expected in the long term.

PROPOSAL FOR RESTRICTION

Experts from the BfR, the German Federal Institute for Occupational Safety and Health (BAuA) and the German Federal Environment Agency (UBA), together with colleagues from Denmark, the Netherlands, Norway and Sweden, have spent three years assessing the entire group of substances with regard to the risks to humans and the environment and have sought the expertise of industry associations and manufacturers. The result: a restriction dossier of more than 1,500 pages.

PROTECTION FOR PEOPLE AND THE ENVIRONMENT

According to the European Chemicals Regulation REACH, a restriction procedure is initiated if an unacceptable, inadequately controlled risk is established for a substance. For PFAS, this is mainly due to their extreme persistence. It is estimated that around 4.5 million tonnes of PFAS will be released into the environment over the next 30 years if no restrictions are imposed. In the decision-making process, the risks to humans and the environment are compared with those posed by the available alternatives and weighed against the economic consequences and social significance of the substances.

The dossier was submitted to the European Chemicals Agency (ECHA) for review in January 2023. The aim is a comprehensive ban on the production, use and placing on the market of the entire group of substances and not just individual PFAS. The idea is to prevent the uncontrolled use of “substitute PFAS” with only slight changes to the molecular structure. A recommendation from ECHA’s scientific committees should be submitted to the EU Commission for a final decision by 2024 at the latest. If the PFAS restriction proposal is adopted, this would be one of the most comprehensive bans on chemical substances since the European chemicals legislation (REACH Regulation) entered into force in 2007.

The dossier also contains recommendations for measures, exemptions for important areas and technologies as well as transitional periods. This means that manufacturers have time to develop sustainable alternatives, and there are already some, meaning that nothing stands in the way of the use of takeaway cups and the rest in the future. —

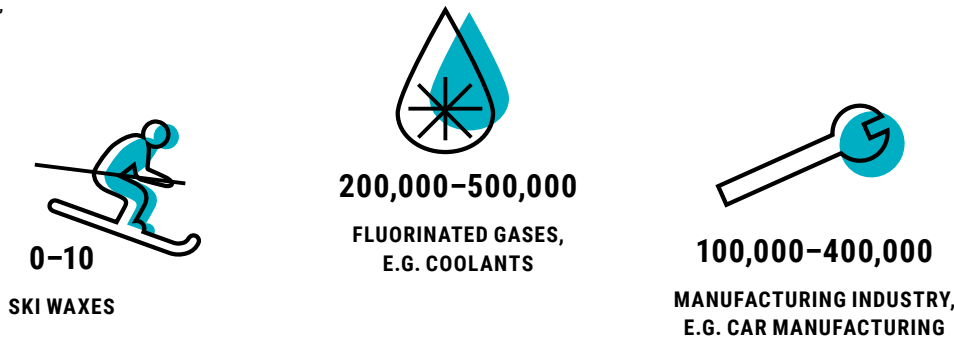
SUPPOSED MIRACLE PRODUCT WITH A DARK SIDE

PFAS are used in many products because of their unique properties. These include coolants, textiles, cooking utensils, food packaging and electronic devices. They are now detectable in the environment and in humans. It is known from animal experiments that many PFAS in higher doses can damage unborn babies and the liver as well as impair lipid metabolism, thyroid hormone levels and the immune system. It has been observed in children with elevated PFAS concentrations in their blood that comparatively lower concentrations of antibodies are formed after vaccinations. Some of the substances are also suspected of being carcinogenic. However, no human data or data on the prediction of adverse health effects is available for the majority of the compounds.

More information



BfR information “PFAS”



HOW MANY TONNES OF PFAS ARE RELEASED INTO THE ENVIRONMENT EACH YEAR?



Understanding the beginning

Tissue cultures intended to “simulate” pregnancy and enable testing of potentially risky chemicals – without animal experiments.



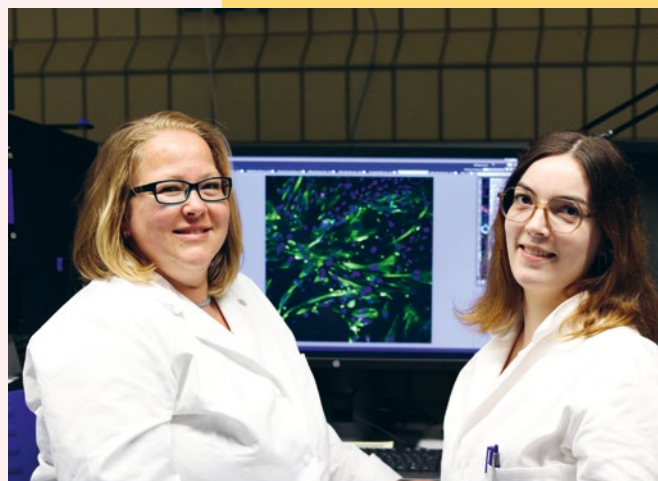
An unborn being is a sensitive creature. Approximately two in five pregnancies end prematurely, 80 percent of these during the first three months. In its early stages, the embryo is particularly vulnerable. Chemical substances are one of the reasons for unwanted miscarriages as well as abnormalities or developmental disorders. The clearest example is the thalidomide catastrophe: in the 1960s, the active ingredient prescribed against morning sickness for pregnant women in the first three months of pregnancy caused severe organ damage and missing limbs in babies.

Since the thalidomide catastrophe, chemicals and drugs must be tested for harm to the unborn baby before being put on the market. This is still predominantly done using animal experiments. At the German Centre for the Protection of Laboratory Animals (Bf3R), which is part of the German Federal Institute for Risk Assessment (BfR), scientists Dr Fanny Knöspel and Mirjam Niethammer are working on an alternative – embryoids from mouse cells. “Embryoids are embryo-like tissues created from stem cells,” explains Fanny Knöspel. “We want to understand how an embryo implants in the uterus and how substances affect this process and embryonic development.”

FEWER OFFSPRING – A WARNING SIGNAL

Established and legally required tests for testing chemical substances, such as pesticides, are usually carried out on rats and rabbits. The parental generation receives the test substance, for example with their food, to identify possible poisonous (toxic) effects on their offspring. It is then determined whether there are any health consequences, for example, whether the number of offspring decreases or if abnormalities and growth disorders develop.

One of the disadvantages of these tests is the fact that results from one animal species can only partially be transferred to others or to humans. This can mean that a dangerous substance is not detected – or, conversely, that a potentially useful drug is discarded as a seemingly harmful substance. And, of course, live animals are required for these experiments. The development of alternative methods by the Bf3R can help to reduce the number of laboratory animals in this area.



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“We want to understand how an embryo implants in the uterus and how substances affect this process and embryonic development.”

DR FANNY KNÖSPEL (LEFT SIDE) AND
MIRJAM NIETHAMMER, BfR

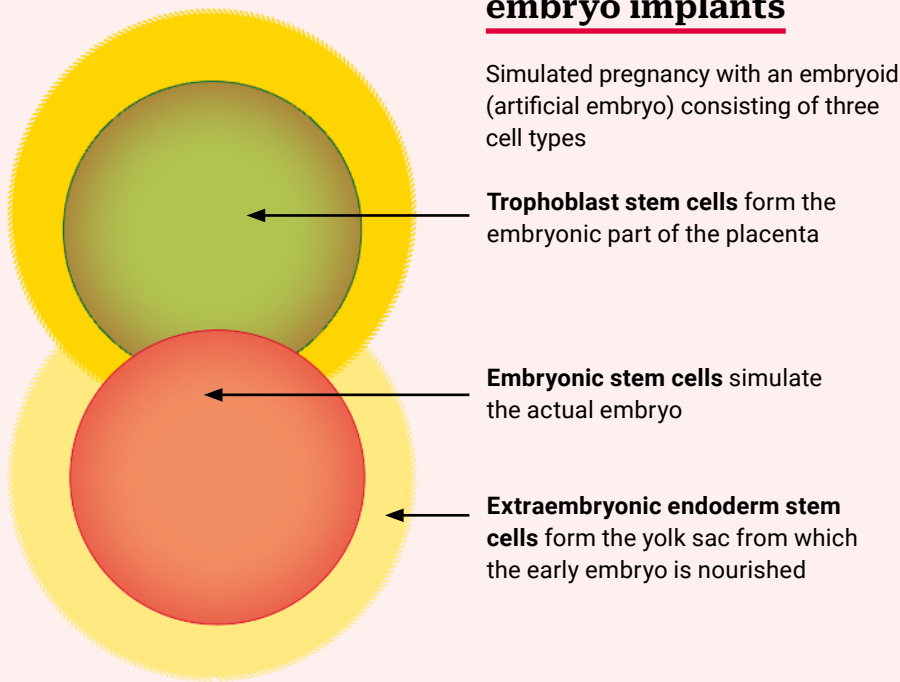
TESTS ON CELLS INSTEAD OF ANIMALS

Three alternative methods have already been independently tested (validated) in the past to ensure their suitability. They do not test living animals (in vivo) but work with cell and tissue cultures (in vitro).

The methods are based on rat embryos, connective tissue cells obtained from these and embryonic stem cells from mouse embryos. However, all three test systems are subject to significant limitations and have not yet become established methods. “A common cause of a pregnancy ending prematurely are interaction problems between the embryo and the mother’s uterus,” says Knöspel. “However, the existing test methods do not allow us to better understand these processes.”

Knöspel and Niethammer want to use an animal-free model to better understand how the uterine lining and the embryo communicate with each other. They are

Researching how an embryo implants



also investigating the extent to which medication and chemicals can influence the implantation of the early embryo in the uterus. These are ambitious goals that the two scientists want to achieve.

The first stage involves creating the embryo-like embryooids and a tissue culture from the uterine lining (endometrium) and connective tissue. The researchers are adopting a two-pronged strategy: Knöspel is focusing on the embryooids, Niethammer on the endometrium. They will only be combined when both biological models work on their own. However, it has not yet progressed that far.

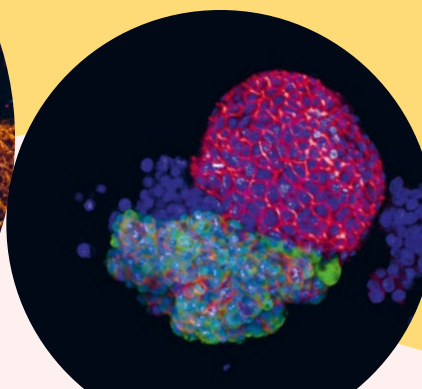
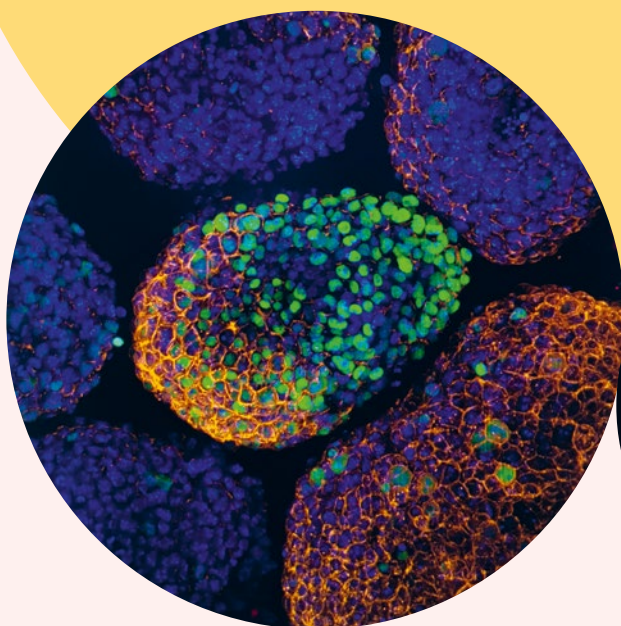
THREE CELL TYPES FORM THE EMBRYO

Fanny Knöspel works with three different cell types. Two of them were originally isolated from the early embryo (blastocyst) of a mouse. They are now stably cultivated as stem cells in a petri dish. Depending on their stage of development, stem cells have the ability to transform (differentiate) into different cell types. This ability has made it possible to obtain the third cell type. Stem cells can also multiply almost indefinitely. Therefore, they are a very good source for developing animal-free testing methods.

“We put these cells together in a nutrient solution and then something astonishing happens – the cells organise themselves into embryo-like structures,” reports Fanny Knöspel. “This allows us to study the first stages of development, such as the formation of the amniotic sac, the amniotic cavity and the cotyledons, from which the organs then develop.” So far, the embryooids have been kept alive for around a week.

CELL STRESS AND CELL DEATH

Even though it would be more realistic to study the embryooids on the uterine lining, they can also be tested directly for damage caused by potentially toxic substances. To do this, the cell structures are exposed to the chemical under investigation for one to two days.



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The cells organise themselves independently into embryo-like structures and demonstrate the first stages of development, such as the formation of the amniotic cavity.

“We then look to see if we can detect any changes,” says Knöspel. “These can be obvious processes such as the death of the cells, or we can observe metabolic processes that suggest increased stress.”

The creation of “artificial” embryos is already an established field of research. When it comes to attempts to recreate a uterus on a microscopic scale, the situation is different. They are still in their infancy, as it were. It is proving much more difficult to grow stable uterine cells. Another question is whether the uterine cells grow on a stabilising network of connective tissue as a basis (matrix) or whether they can form this independently, which would be closer to nature.

“Our aim is to depict the superficial mucous membrane with the associated connective tissue for the uterus-like structure,” says Mirjam Niethammer. Another important factor for the successful “implantation” of an embryo are hormones, which are essential for a prospective pregnancy in the “real” uterus. “Of course, an artificial system consisting of embryo-like and uterine tissue would still be far from a perfect representation of nature,” summarises Knöspel. “But then we are already dealing with five different cell types that have to fit together and harmonise.” There is no doubt that the two scientists have set themselves some ambitious goals to investigate nature – and to detect substances that pose a risk to the unborn child. —

More information



Niethammer, M. et al. 2022. **In vitro models of human development and their potential application in developmental toxicity testing.** *Development* 149 (20). DOI: 10.1242/dev.200933



Ban, Z. et al. 2020. **Shedding light into the black box: Advances in in vitro systems for studying implantation.** *Developmental Biology* 463 (1): 1-10. DOI: 10.1016/j.ydbio.2020.04.003.

INTERNATIONAL NEWS



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From theory to practice

Since 2016, the EFSA Advisory Forum and EFSA have been discussing how education, advanced training and vocational training in risk assessment can be expanded. The German EFSA Focal Point at the BfR is now working with representatives from eight other member states to develop a quality seal for training courses. The aim is to make high-quality training courses more visible and boost risk assessment worldwide.

Greater food safety in Tunisia

BfR President Professor Dr Dr Andreas Hensel chaired the first meeting of the steering committee with the Health Minister of Tunisia (in photo left) in May 2023 as part of the cooperation for greater food safety and consumer health protection in Tunisia. Representatives from Tunisian institutions and German

federal authorities discussed the second half of the project. The aim is to involve public administration, science, business and civil society more closely in future.

More information



BfR press release
"German-Tunisian cooperation for increased food safety"



© Health Ministry of Tunisia

INTERNAL AFFAIRS

Excellence

Professor Dr Peter Furst has been a BfR Maria Sibylla Merian fellow since April 2023. The internationally renowned food chemist has been advising the BfR for many years with a wealth of valuable expertise. As part of the fellowship, Professor Furst is researching the behaviour of undesirable substances and their transformation products along the food chain. These include the development of new chemical analytical methods as well as replacement and supplementary methods for animal feed experiments.

More information



Press release
"How are impurities modified during the food production process?" (pdf)

From the BfR to the EU Commission

Dr Jasmina Vandrich was delegated to the EU Commission's Directorate-General for Research and Innovation food systems unit as part of the professional development programme for public-sector employees. She was involved in the publication on the transformation of the urban food system, which will be incorporated into the new "Food 2030 Pathways for Action" following the EU's "Food 2030" conference in December 2023. One focus will be future food safety systems.

More information



European Commission, Directorate-General for Research and Innovation, Luth, D., Vandrich, J., Fabbri, K., **Urban food system transformation in the context of Food 2030: current practice & outlook towards 2030**, Vandrich, J.(editor), Fabbri, K.(editor), Publications Office of the European Union, 2023, <https://data.europa.eu/doi/10.2777/507125>



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A visit to Morocco

BfR Vice President Professor Dr Tanja Schwerdtle (centre photo) attended the agricultural fair in Meknès, Morocco in May 2023 and met with representatives from the Moroccan Food Safety Authority (ONSSA). In addition to a laboratory visit, the meeting focused on the cooperation's strategic direction. The BfR and ONSSA have been cooperating on consumer health protection since 2019.

INTERNA

Young scientists wanted

At the annual meeting of the German Academic International Network (GAIN) in Boston in August 2023, the BfR joined together with the Federal Institute for Materials Research and Testing (BAM) to recruit new talent. Departmental research institutions like the BfR need scientists at the highest international level for research and work in risk assessment and policy advice. At the same time, they offer young scientists practical and interdisciplinary research at the interface with politics, business and society.



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